Re-evaluating Pharmaceutical Pipelines

Emerging Markets, Biologics and Orphan Drugs to Shape Future Decision Making
GBI Research Report Guidance

- The report comprises an executive summary capturing the key points - Adopting new business models, drug attrition vs. business strategy, R&D challenges and opportunities
- The chapter titled R&D trends provides FDA approval rates and R&D expenditure, strategies to reduce failure rates in Phase III and maximizing product portfolio.
- The chapter titled R&D challenges and opportunities discusses the geographical therapeutic and business diversification along with the list of drugs losing patent between 2011 and 2013
- The chapter titled Mergers, acquisitions and partnerships discusses major mergers, acquisitions, collaborations and partnerships along with the company analysis.
- The chapter titled Market outlook discusses - Investing for the future, conflicts in the business model, cost-effectiveness of drugs.
Executive Summary

GBI Research, a leading business intelligence provider, has released its latest research, “Re-evaluating Pharmaceutical Pipelines: Investing for the Future”, which examines the key issues influencing the re-evaluation of pharmaceutical pipelines and the strategies the industry has adopted to address both internal and external challenges. It provides an overview of the factors impacting the pharmaceuticals industry, the economic environment, the emergence of new markets, recent M&A and partnering activity, and the recent advances in science and technology that are driving companies to re-evaluate their pipelines. It discusses trends in pharma productivity, the impact of drug attrition rates on different drug therapies and business strategies, and highlights the strategies companies have adopted to reduce failure rates in Phase III development and maximize their product portfolios. In addition, it discusses the different strategies companies have adopted to refine their pipelines in order to ensure future growth and shareholder value alongside internal improvement on R&D efficiency. The report provides an overview of different strategies available to companies to acquire, partner or license products as they re-evaluate their pipelines. It includes profiles and detailed analysis of the leading pharmaceutical companies and examines their pipelines, M&A and partnering activity, and pharma R&D growth strategies. Finally, it raises questions regarding the future outlook of the market and the ways in which pharma needs to re-evaluate its product pipelines to secure future growth.

Adopting New Business Models

According to Tufts Center for the Study of Drug Development (CSDD), drug developers are changing the way they perform R&D, “placing a greater reliance on translational science to identify the right disease target(s) for new molecules; greater use of partnering with external service providers to share risks, reduce cycle times, lower costs and improve resource management, and greater use of sophisticated portfolio management techniques.”

Industry leaders argue that the productivity crisis which pharma has faced has been due to its closed innovation systems, which relied primarily on utilizing in-house expertise to address the challenges faced by product research and development. However, during the last decade pharma has actively embraced an open innovation R&D paradigm, establishing cooperative alliances, partnerships and joint ventures with research and technology specialists to license in and spin out expertise/technologies, acquiring and divesting technologies and products to help develop proactive solutions and expand their potential markets. This has become particularly pertinent as companies redirect their R&D budgets and invest overseas into new scientific hubs in China and India, and where there has been a strategic shift of funds out of research and into product development. Meanwhile, leading academic institutions have been actively patenting their research discoveries as Big Pharma starts knocking on their doors looking for alternative routes for innovation.
Drug Attrition vs. Business Strategy

In 2008, Czerepak and Ryser investigated the origins of drugs approved by the FDA and those failing in Phase III during the period January 2006 to December 2007, from small, medium and large pharma. Of the XX FDA approvals, XX% were from biotech, XX% from pharma-biotech relationships, and XX% from pharmaceutical companies (four licensed/acquired from pharma). Interestingly, only XX% of products were new chemical entities/novel drugs, XX% were line extensions, and 40% were “me-toos”.

According to this dataset, more than XX% of novel drug approvals were originally generated by the biotech industry, and over XX% of approvals in the line-extension and me-too category came from the biotech industry. Interestingly, for each FDA approval there was, on average, one Phase III failure, and XX% of these failures were products originating from biotech companies. Overall, during 2006 and 2007, the pharmaceutical industry had a much better success rate than biotech companies in getting drugs approved in the US, however, XX% of all pharmaceutical companies’ approved products were sourced from the biotech industry, either through collaborations or acquisitions.
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2 Introduction

2.1 Market Conditions

“Global drug makers face an extremely turbulent decade from which only highly innovative medicine makers and large-volume generics makers will emerge, with players who try to occupy the middle ground largely disappearing.”

Severin Schwan, the chief executive of Roche Holding AG

Wall Street Journal, December 6, 2011

The healthcare industry is undergoing a dramatic change; it faces many challenges and new opportunities to create new and innovative medicines to address unmet clinical needs. Whilst the pharmaceutical market was estimated to be worth around $XX billion in 2011 (IMAP, 2011), growth during the period 2011-2015 is forecast to remain in the mid single digits, as leading brands face generic erosion, drug pricing pressures and healthcare reforms, and begin to benefit from the organic growth in the emerging markets. By 2015, there will be a strategic shift in the use of medicines throughout the globe, with growth in the emerging markets outstripping that of the developed world (the US, Europe and Japan).

Pharma companies have seized new opportunities for growth as emerging consumers struggle to gain access to cost-effective and affordable drugs. In the current environment, local generics and biosimilar manufacturers have thrived. In order to compete, multinational companies will need to establish local and national distribution networks, as well as gaining a greater understanding of the regulatory frameworks and local medical needs to increase patient access to a broader range of innovative drugs.

Government payers will increasingly influence which drugs patients will have access to as they undertake healthcare reforms and implement new legislation and stringent regulations. Cost-containment will be paramount as governments try to restrain their healthcare budgets, placing a greater pressure on companies to reduce drug prices and a greater onus on the patient to pay for their medicines. In turn, patient empowerment will place a greater burden on healthcare companies to educate patients and differentiate their products from those of their competitors.

Since 2000, the pharma industry has witnessed a wave of consolidation, and this trend is set to continue as cash-rich pharma companies look to plug their pipeline gaps and optimize their product management lifecycles as they reel from a series of multibillion patent expirations. In the near-term, this will largely be achieved through strategic mergers of established partnerships and acquisitions of innovative biotechs which have been struggling to secure private equity investment.

There will continue to be new opportunities in the personalization of medicines as companies target areas of significant unmet clinical need, and this should stimulate growth in the development of biologics, orphan drugs, and the emergence of therapeutic vaccines. In order to remain ahead of the curve, pharma companies must invest in fundamental science and technologies to drive innovation from within, adopting new in vivo, in vitro and in silico technologies to optimize drug design, coupled with preclinical and clinical biomarkers and advances in bioinformatics and model simulations to help de-risk and improve intelligent product development.

In the long-term, true value will only be created through differentiated products (first-in-class or best-in-class medicines), which address specific medical needs. Companies will need to jump through additional hoops to ensure safety, efficacy and cost-effectiveness of new products as regulators become more stringent on product approvals and governments become more cost conscious.

The following section briefly discusses some of the key factors that have influenced the performance of the pharmaceutical industry during the last 24 months and will continue to impact the market going forward.
2.4.3 Trends in 2011

M&A and partnering activity throughout 2011 remained fairly constant, with around XX M&A deals per month versus XX partnerships indicating that the industry continues to seek external alliances and strategic acquisition to innovate and drive future growth.

Figure 5: Re-evaluating Pharmaceutical Pipelines, M&A versus Partnering Activity, 2011

The vast majority of these strategic partnerships have involved technologies or products in discovery and preclinical development, or the commercialization and distribution of a product once they have reached the market.
3.1.3 Strategies to Reduce Failure Rates in Phase III

Several groups have shown that the majority of products fail as they migrate from Phase II to Phase III development (DiMasi & Grabowski, 2007; Kola & Landis, 2004). According to Kola and Landis, most product failures in late stage clinical development occur due to poor pharmacokinetics, lack of efficacy and clinical safety, however, during the period 1991 to 2000 the industry appeared to become more effective in improving pharmacokinetics (Kola & Landis, 2004; Figure 18).

Late-stage clinical trials account for a large proportion of the drug development costs, and if a drug fails at this stage it can attract large out-of-pocket investment, tying up capital resources and time. Pharmaceutical companies have developed a number of strategies to identify as early as possible which drugs may eventually fail. Small improvements during the early phases of drug development can have a major impact on productivity and the utility of resources. It has been estimated that terminating just XX% of Phase III failures in Phase I could reduce out-of-pocket clinical costs by XX% to XX% (Schachter and Ramoni, 2007).

To overcome the high costs of attrition, the industry has been introducing various new technology tools, including genomics, proteomics, high-throughput screening, metabolomics, bioinformatics and molecular imaging to improve the identification and validation of new chemical entities.

![Figure 18: Re-evaluating Pharmaceutical Pipelines, Reasons for Drug Failure in Late-stage Development, 1991 and 2000](source)

Source: Modified from Kola and Landis, 2004
4.5 OTC Medicines

Since the late 1970s, pharmaceutical companies have been actively switching prescription (Rx) products to over-the-counter (OTC) status, helping to expand product accessibility and optimize their product lifecycle management (PLM). More than 100 prescription products have been switched to OTC, and many more are under review. According to the US Food and Drug Administration (FDA), “XX out of every ten medications bought by US consumers are OTC drugs.”

In 2010, the global OTC market was estimated to be worth around $XX billion, growing at around XX% per annum, approximately a tenth of the size of the overall pharmaceutical market. The US and western Europe account for nearly XX% of sales, and Japan accounts for around XX% of revenues. While the emerging economies are a relatively small segment of the market, their growth during the last few years has superseded the rest of the market. The stabilization and economic growth and “OTC friendly environment” of many Asian and Eastern European Countries such as China, Russia, Romania, and Poland are providing new opportunities for OTC development (Figure 33).

Figure 33: Re-evaluating Pharmaceutical Pipelines, Geographical Sales Split of the OTC Market, (%), 2010

Source: GBI Research, AESGP, 2011
8 Appendix

8.1 Market Definition

Some of the terms used in this report are described below:

**Biosimilar** - Also known as a follow-on biologic; the term is used to describe officially-approved subsequent versions of innovator biopharmaceutical products made by a different sponsor following patent and exclusivity expiry on the innovator product.

**Biologic** - A medicinal preparation made from living organisms and their products, such as a serum or vaccine, therapeutic protein or monoclonal antibody.

**Generic** - A drug which is produced and distributed without patent protection. The generic drug may still have a patent on the formulation but not on the active ingredient.

**Orphan drugs** - A drug that has been developed specifically to treat a rare medical condition, the condition itself being referred to as an orphan disease.

**Over-the-counter (OTC) drug** - Medicines which can be obtained without a doctor’s prescription.

**Emerging markets** - New marketplaces that are emerging for the pharmaceutical industry to invest in due to the stabilization of the economic and political environment within the countries, which has resulted in rising levels of healthcare access and funding. Countries often included in this term include the BRIC economies (Brazil, Russia, India and China), which are often termed the first-tier emerging countries, followed by Argentina, Egypt, Indonesia, Mexico, Pakistan, Poland, Romania, South Africa, Turkey, Thailand, Vietnam, Ukraine and Venezuela.

8.2 Abbreviations

**ADMET** - Absorption, Distribution, Metabolism, Elimination, Toxicology

**AESGP** - Association of the European Self-Medication Industry

**AH** - Pulmonary Arterial Hypertension

**CAGR** - Compounded Annual Growth Rate

**CDER** - Center for Drug Evaluation and Research

**CHMP** - Committee for Medicinal Products for Human Use

**CMO** - Clinical Management Organizations

**CNS** - Central Nervous System

**COPD** - Chronic Obstructive Pulmonary Disease

**CRADA** - Cooperative Research and Development Agreement

**CRO** - Clinical Research Organizations

**DNA** - Deoxyribonucleic acid

**DRP** - Drug Reprofiling Platform

**EC** - European Commission

**EMA** - European Medicine Agency

**EU** - European Union

**FDA** - US Food and Drug Administration

**GI** - Gastrointestinal

**GSK** - GlaxoSmithKline

**HEA** - Hereditary Angioedema

**HPV** - Human Papillomavirus
8.3 Sources

Appendix

- De Ridder F (2005) Predicting the Outcome of Phase III Trials using Phase II Data: A Case Study of Clinical Trial Simulation in Late Stage Drug Development *Basic & Clinical Pharmacology & Toxicology* Volume 96, Issue 3, pages 235-241, March 2005
- Institute of Medicine (2010) Rare Diseases and Orphan Products: Accelerating Research and Development


### 8.4 Methodology

GBI Research’s dedicated Research and Analysis Teams consist of experienced professionals with a pedigree in marketing, market research, consulting backgrounds in the medical devices industry and advanced statistical expertise.

GBI Research adheres to the Codes of Practice of the Market Research Society (www.mrs.org.uk) and the Strategic and Competitive Intelligence Professionals (www.scip.org).

All GBI Research databases are continuously updated and revised. The following research methodology is followed for all databases and reports.

### 8.4.1 Primary Research

Primary research involves e-mail correspondence, telephone interviews, as well as face-to-face interviews for each market, category, segment and sub-segment across geographies.

Key opinion leaders: physicians and surgeons specializing in different therapeutic areas corresponding to different kinds of pharmaceutical drugs.

The following sources were referred to in addition to company reports and websites:

- Company Websites
- Product Websites
- Company Annual Reports
Appendix

- Food and Drug Administration
- European Medicine Agency

8.4.2 Secondary Research

Secondary research was carried out on internal and external sources to source qualitative and quantitative information in the report.

The secondary research sources that are referred in this report include, but are not limited to:

Company websites, annual reports, financial reports, investor presentations and SEC Filings for the twenty companies covered in this report;

- Industry trade journals, scientific journals and other technical literature;
- Relevant patent and regulatory databases;
- National government documents, statistical databases and market reports; and
- News articles, press releases and web-casts specific to the companies operating in the market.

8.6 Disclaimer

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